Smith (W. E)

HEREDITARY OR DEGENERATIVE ATAXIA:

SIX CASES IN ONE FAMILY: DEATH OF ONE CASE AND AUTOPSY.

BY

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HEREDITARY OR DEGENERATIVE ATAXIA. SIX CASES IN ONE FAMILY. — DEATH OF ONE CASE, AND AUTOPSY.[1]

"Diese Befunde sind vielleicht im Stande ein Licht auf die Entstehungsweise der hereditären Nervenkrankheiten zu werfen. Diese treten unter den Begriff der Bildungshemmungen."
Möbius: Ueber die hereditäre Ataxie.

FAMILY HISTORY: The patients to be considered in this paper are J. W. W. (father), Emma, Alice, Clara, Jessie, and Myra (daughters). There have been thirteen children in the family, eight girls and five boys. Two of the girls died years ago unmarried; one at the age of sixteen from acute meningitis, the result of injury, the other (Alice) at the age of twenty-five, with symptoms, so far as I can ascertain, exactly like the symptoms I shall describe in her sisters. I never knew them. One daughter left home at the age of fourteen. She is married and has always been strong and healthy, but has an anæmic child about twelve years old, who for years has been obliged to wear a mechanical support upon one of her ankles. The remaining five daughters are unmarried and have always lived with their parents. Their ages, when I first met them in October, 1882, were thirty-seven, twenty-nine, twenty-seven, fifteen and fourteen respectively. At this time the oldest son was thirty-five (married and the father of young and anæmic children), and the youngest son seventeen; all the sons were well developed, strong and healthy, except possibly the oldest, who in 1881 cut his foot with an axe and barely escaped death from tetanus; since then he has never been well.

[1] Read by invitation, before the Section for Clinical Medicine, Pathology, and Hygiene, Suffolk District Medical Society, June 9, 1885.

The family upon both the father's and mother's side is long-lived and healthy, with no history of consanguineous marriages, insanity, syphilis, or any inherited disease that I can ascertain by the most careful inquiry. The family of Mr. W. is, however, peculiarly nervous and excitable and has a marked history of drunkenness in the two previous generations: his father may possibly have had ataxic symptoms before his death, although the history is not quite clear; his mother had the rickets when a girl and was of a very quarrelsome disposition in the latter years of her life, while he has a brother who lacks all moral sense and is now serving a long sentence in the State Prison for aggravated assault. None of the present generation have ever used liquor of any kind, either habitually or to excess.

In the family of the mother, too, there is an instance of some undetermined nervous peculiarity. A niece, now twenty-one, has for the last ten years been able to walk only by the aid of a mechanical support upon the right ankle, while for the last five years she has been practically without the use of the right wrist and hand from some unaccountable weakness which invaded them insidiously and without assignable cause.

The boys, as I have said, are and always have been well. When, however, the girls have reached the age of six or seven, they all, with three exceptions — the one who died from meningitis, the married one and the youngest who is now (June, 1885), aged sixteen — have developed a series of morbid symptoms regular in order and progression. The first symptoms noticed by them have been gastric disturbances and palpitation of the heart, followed by an unsteady gait which later became purely ataxic. This ataxia gradually extends to the hands; and here the disease seems to remain stationary for an indefinite period of

time. I will describe the cases as I saw them in October, 1882.

Clinical History: Case I. Emma, aged thirty-seven, when a child was bright and quick at figures. At about the age of six she began to manifest a weakness in the lower limbs and an ataxic gait. Of earlier symptoms no definite record can be obtained from her, since she is tongue-tied, has lost the power of articulation and can utter only a sort of guttural laugh. The general history of the case, however, is pretty clear. The muscular weakness gradually invaded the upper extremities causing a "wrist drop," and an incoördination of movement in the hands. At about the same time, or a little later, her younger sister, Alice, began to develop similar ataxic symptoms and complain of muscular weakness.

Upon analysis of the drinking-water made at this time (1862) by Dr. Geo. Rice, of Framingham, and Dr. Hayes, of Boston, lead was detected in considerable amount. The urine was not examined. In deference to medical opinion the lead pipe then used to convey the water from the well was at once removed. Gutta-percha pipe was put in its place but proving unsatisfactory was soon superseded by earthern-ware pipe. In 1874 the well itself was abandoned and the supply of water has since been brought in tin-lined pipes from a new spring upon a distant hill. This water I have carefully analyzed but can find no lead in it. Nor have I ever been able to find lead in the urine of any member of the family.

In spite, however, of all precautions the ataxic symptoms not only continued to increase but even attacked new patients (always the girls) in the family, some of whom had never used the suspected water from the old well. Alice died in 1871. Before her death she had suffered greatly from gastric and abdo-

minal pain. Her final illness was about three weeks in duration and was characterized by spinal pain and by muscular spasms and contractures. She died in convulsions. I never knew her.

Emma, a helpless creature, still lives and sits or half reclines in a large chair most of the time.

She has an excessive right lateral curvature of the spine combined with cyphosis, her feet are enlarged and fixed immovably in the position of equino-varus, even the slightest passive movement at the ankle-joint being no longer possible, the hands are flexed upon

the forearm and the head rests helpless upon the chest. Her position is perfectly shown in the accompanying photographs.[2] There is complete paralysis of the lower limbs and only the slightest possible voluntary but still wholly incoördinate movement of the hands. She can neither pick up objects from her lap nor hold them when placed in her hand. Her legs often jerk involuntarily.

Electro sensibility is greatly decreased. Electro irritability, as tested with the faradic current is decreased, but increased even to spasms with the galvanic (5 cells. Stöhrer). The left side of the body is less responsive than the right and the lower extremities less than the upper to electrical stimuli. The tendon reflexes are wholly absent but *the plantar reflex is present* and she has never had any girdle sensation. The cutaneous circulation is low and the feet and ankles are usually purple with congestion. There is a partial facial paralysis so that saliva constantly flows from the mouth. The muscles of deglutition are so impaired in their action that it is impossible for her to masticate food and almost impossible for her to swallow either food or drink. There is no atrophy of the optic disk; no paralysis of sphincters of rectum or bladder and no tendency to bed sores.

For the past fifteen years she has been subject to frequent epileptic attacks and to painful muscular spasms and contractures in the lower extremities. She is irritable at times, becomes much excited if her desires are not immediately comprehended and will often shout for hours for no apparent reason. She takes note of her surroundings and is keenly sensitive to comments that are made upon her; gives considerable evidence of intelligence and attempts to read the

[2] The photographs are true to life in showing the peculiar "chopped off" appearance of the toes and the marked enlargement of the feet. This is *not* the fault of perspective.

papers, calling attention to items that particularly interest her.

In May, 1885, I re-examined her and find that although it has been nearly a year since she has had an epileptic convulsion she has for six months been markedly losing strength. She no longer cares to read, is suffering from palpitation of the heart and gastric trouble, begins to complain of considerable pain and shows an increasing prostration. She represents the completest development of the disease as it has occurred in this series of cases.

Case III. Clara, aged twenty-nine, had seemed to her parents a child of ordinary health until she reached the age of nine or ten, when she began to complain at times of palpitation of the heart, of dyspnœa and of muscular weakness in the lower limbs. When she was sixteen she had what was called a "gastric fever." She did not remember that she had ever had any colic pains or fleeting pains in the joints, but had suffered greatly from acidity of stomach and nausea.

Soon after these initiatory symptoms of palpitation and muscular weakness, she began to notice that she had the same peculiar gait that she had seen in her sisters, Emma and Alice, and *later* the same incoördination of movement in her arms and hands. This was about 1869. Soon walking upstairs became almost impossible from inability to raise the feet high enough. About eight years ago she had a sickness marked by headache and pain along the spine; was delirious for nearly a fortnight. Since that time she has been duller than before and more inclined to doze and sleep.

When first I saw her in October, 1882, she was in a prostrated condition without fever. Pulse 140, but scarcely to be detected at the wrist. Dyspnœa excessive. She complained of lassitude, headache and nausea, of a burning heat in the legs, and of a girdle sen-

sation that seemed like a band of about a hand's breadth becoming tighter and tighter around her. This state of prostration lasted about a week, at the end of which time I could make a more careful study of the case. She was very anæmic and had right lateral curvature of the spine together with cyphosis. She complained of vertigo, and of a dull, heavy feeling at the base of the skull. There was almost complete paresis of the lower extremities, both feet were in position of equino-varus and ankles as immovable as though ankylosed. The muscles of the thighs and calves of legs had become so contracted that the lower limbs were much distorted. Her photograph would have looked not unlike the photographs of her sister Emma.

In the upper extremities, the muscles of the hand, and especially the ball of the thumb, did not seem so wasted as did other parts of the muscular system. Has had a "wrist drop" for a number of years, although she could easily raise the hand upon the wrist and supinate it. She could raise the arm only slightly and with the greatest difficulty; could not raise it level with the shoulder. The muscles of the trunk had so far lost their power that she could not sit securely in her chair, but "slouched down" and tended constantly to slip out; she then had not the power to lift herself back into place.

There was no facial paralysis and she could protrude the tongue normally. Deglutition, however, was often extremely difficult and a well-marked tremor of the head was called forth by attempts at voluntary movements. There was a marked peculiarity in her speech, the voice often degenerated into a mere whisper and the words came always slowly and rythmically like the "scanning speech" of multiple sclerosis. The simplest mental acts were the result of laborious effort; there

was always a tardy response to questions because she required time to comprehend one's meaning clearly and memory had become exceedingly defective.

The vitality of the skin, especially in the lower extremities, was very feeble and feet and ankles were markedly congested. She complained greatly of "chilblains." The skin in the beginning of her disease used to be hyperæsthetic, but for six years had been growing anæsthetic, so that she now could scarcely distinguish whether I was pinching, pricking, tickling, or merely rubbing the skin with the ends of my fingers. When, however, she had recognized that her skin was touched, a mental process requiring usually several seconds of time, she said she felt the contact more keenly than she used to feel it and that the sensation lasted longer than it used to last. Sometimes the slightest impression would cause local muscular spasms. Frequently when sitting, but especially in bed, the legs would jerk and flex so powerfully that she would beg to have weights put upon the knees to keep them down. Tendon reflexes entirely absent; no ankle clonus. She often had the sense of formication in the trunk and lower extremities and of a tingling in the ends of the fingers. Her hearing had become very defective and vision was confused. In watching a carriage pass the window she said she could not distinguish between the front and the hind wheels; the front wheels seemed to be where the hind wheels ought to be, but where the hind wheels were she could not tell. There was a marked chromatic aberration and also nystagmus. No strabismus. Muscæ volitantes were almost constantly seen and caused her great annoyance. The pupils seemed normal in size and reaction to light. There was no atrophy of the optic disk that I could distinguish by an ophthalmoscopic examination.

After securing a generous diet and various tonic remedies, I attempted, in December, 1882, to relieve in some measure the contractures in the lower extremities. Another attack of collapse, however, interfered for a time with any active treatment. Later I began to apply electricity and was surprised to note the rapid increase of strength in the back and lower limbs. In January, 1883, I applied a plaster jacket temporarily to the trunk and thereby gave the muscles of the back so much support that she regained the power of raising herself from the chair without assistance, and of standing upon her feet. A little later I applied silicate bandages to the feet and gradually got the ankle-joints flexible and the feet in fair position. She could now move them readily and even raise them from the floor so that she succeeded in walking a few steps with the aid of her mother.

Among the many varieties of tonic treatment that I tried I will especially mention phosphorus, the phosphide of zinc, strychnia, and the nitrate of silver, finding the silver to yield the best results and giving it in half-grain doses three times a day. Strychnia could not be long continued since the most minute doses quickly produced tetanic spasms and great distress.

Under such care as I have thus briefly outlined, and with the exception of several attacks of dyspnœa, vomiting, and collapse, the patient enjoyed a better degree of health until August, 1883, than she had had for years. She now began to suffer the most intense and agonizing pain along the entire tract of the right sciatic nerve from the lumbar region of the spine to the extremities of the toes. Speedily the symptoms of acute myelitis in the cervical and upper dorsal region were noticed, accompanied at times with a decided tendency to opisthotonos. Another collapse ensued marked by an utter rejection of food and by vomiting independent

of the taking of food so that for about ten days she was fed entirely by rectal injections. For many days she suffered the greatest agony from dyspnœa and a continual palpitation of the heart.

At no time was there or had there ever been any marked irritability of the bladder or abnormality in the urine, any paralysis of the sphincters of either the bladder or rectum, any tendency to bed sores or to sores upon the prominent points of pressure. The powers of life had rapidly failed, however, and death finally put an end to her sufferings quietly and without pain after a final illness of about three weeks.

Autopsy. The autopsy was made by me thirty-six hours after death, in the presence of Dr. Jos. H. Warren, of Boston, and Drs. Z. B. Adams, L. M. Palmer, and E. H. Bigelow, of Framingham. The muscular system was seen, upon inspection, to be markedly wasted, but there was a considerable layer of adipose tissue found over the walls of the abdomen. The omentum was atrophied, stomach and intestines empty. The mucous layer of the stomach was injected to a considerable degree. The right ovary was healthy but upon the left a small cyst was found. Uterus small. Kidneys small but otherwise normal. Bladder healthy. In the thorax there were a few pleuritic adhesions, but the lungs were apparently healthy. There was no abnormal amount of pericardial fluid and no disease of pericardium. The brain for various reasons was not examined.

Upon opening the vertebral column the membranes of the cord were found to be deeply injected and markedly adherent to the bony walls. In section the cord was seen to be asymmetrically atrophied, pale and in local areas softened. Portions of it from the dorsal and lumbar regions were reserved for microscopical examination since they were thought to represent

in a sufficient degree the pathological changes that had taken place. I hardened them in Müller's Fluid, and after an incomplete examination sent portions to Dr. James J. Putnam, Lecturer on Nervous Diseases in Harvard University. To his kindness and attention, and to the patience and skilfulness of Dr. Henry P. Quincy, Instructor in Histology in the Harvard Medical School, in preparing the specimens, I am indebted for the following detailed pathology.

"The four pieces of spinal cord which were sent to me for examination were in a well-hardened condition and comprised the whole or greater part of the lumbar and a little of the lower dorsal regions.

"They were imbedded in celluloidine, and their sections were cut with the microtome, stained with Beale's carmine or hæmatoxyline and mounted in Canada Balsam. Sections were also made and very beautifully stained and mounted according to Weigert's method, by Dr. H. P. Quincy.

"Certain abnormalities in these sections were visible even to the naked eye.

"The *shape of the cord was altered*, apparently from shrinkage of the posterior half, so that the central canal appeared displaced backward.

"The left postero-lateral column in the lumbar region looked as if sliced away in part, although special care had been taken to avoid pressure during hardening.

"Intense sclerotic changes occupied almost the whole of the posterior columns, both antero-lateral pyramid tracts in the dorsal region and the remnant of the crossed lateral tracts in the lumbar region.

"When examined under low powers, the following additional changes were observed: —

"The *central canal* was entirely blocked with round cells which took up the coloring matter of hæmatoxyline, and all trace of columnar lining was gone.

"The *posterior columns* were occupied by a dense connective tissue, as in advanced cases of locomotor ataxia, in which nerve fibres were very sparsely scattered, either singly or in small groups. These nerve fibres were less abundant in the lower dorsal than in the mid-lumbar sections, and, in fact, were almost literally absent in a good part of the sections from the former region.

"That portion of the posterior columns immediately adjoining the posterior commissure was, as is so often the case, relatively little affected.

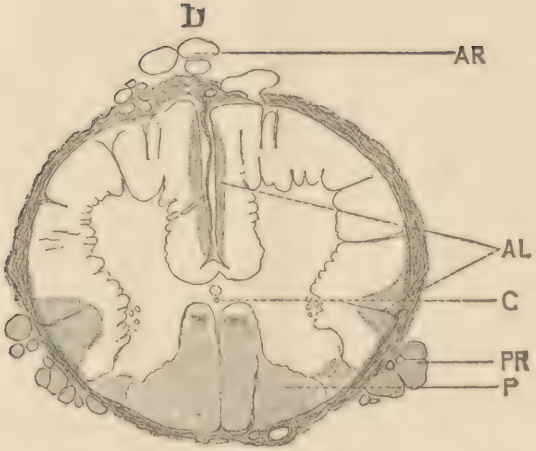
"The *sclerosis of the antero lateral tracts was not so intense* as that of the posterior tracts and posterior nerve roots.

"These changes — increase in the connective tissue, diminution in the number and size of the nerve elements and alteration or disappearance of the myeline — were visible, not only in the posterior columns but to a greater or less extent over the entire section of the fibrous mantle of the cord.

"The *region of the anterior nerve-roots was comparatively healthy*, and strands of apparently healthy axis-cylinders were seen making their way outward from the anterior cornua.

"Compared with the abundant net-work of horizontal motor fibres usually seen in the lumbar enlargement of a healthy cord, the number of those here present was very small. The condition of the posterior as compared with the anterior nerve-roots was strikingly brought out by the Weigert staining. The posterior roots seemed to contain scarcely a single healthy fibre, whereas the fibres of the anterior roots, though somewhat sparse, were relatively abundant.

"The pia mater was thickened over the posterior and lateral columns and the tissue immediately adjoining was more or less sclerosed.



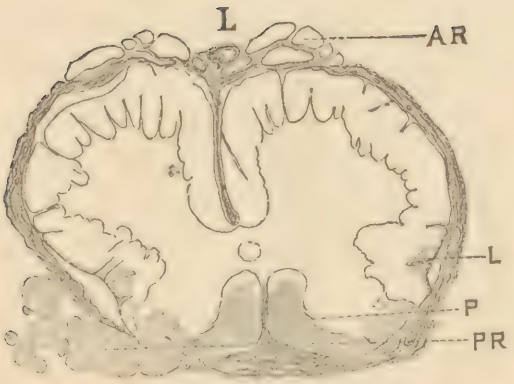
DORSAL REGION.

AR. Anterior nerve roots healthy. AL. Antero-lateral tract diseased.
C. Central Canal. P. Posterior columns diseased.
PR. Posterior nerve roots diseased.

"The *nerve cells of the anterior and posterior cornua* were at all levels *far less numerous* than normal. In some sections only a scattered few were visible, the greater number being in the anterior and lateral groups.

"The cells of the median and internal areas of the anterior cornua were even smaller and paler than usual, and the whole region presented a confused, ill-differentiated appearance. The pericellular spaces looked larger than normal, and although this may have been due to shrinkage during hardening, yet it may be doubted whether such shrinkage would have occurred in a healthy cord.

"A point of anatomical interest was the presence of a *small, supplementary canal* a little posterior to the



LUMBAR REGION.

AR. Anterior nerve roots relatively healthy.
L. Lateral tract diseased. P. Posterior columns diseased.
PR. Posterior nerve roots diseased.

main central canal and separated from it by a thick partition of peri-ependymal tissue. It extended throughout almost the whole of the lumbar region.

"Under still higher powers, it was seen that most of the nerve cells which remained were altered to a greater or less degree and in various ways. Failure to absorb carmine well, absence of processes and a granular texture were common changes. Here and there a small vacuole was seen, in one section a very large one.

"Some cells were reduced to granular masses; a few were globular, pale and homogeneous. The *nucleus* was sometimes entirely absent, sometimes it had entirely lost its outline and was only to be distinguished from the rest of the cells as a reddish flush with the nucleolus in the centre. Sometimes again it was shrunken and angular. The *nucleolus* appeared at times unusually large and dense; in the cases where this was seen, the nucleus, whether by accident or

not, looked shrunken or indistinct. Occasionally no nucleolus was seen.

"Some strands of the *anterior nerve roots* were markedly atrophied while others near them looked comparatively healthy. The myeline was often conspicuously deficient.

"There was no marked hypertrophy of axis cylinders anywhere, but often a moderate increase in size of single fibres, especially in the posterior columns. Atrophied fibres were very common, and on the whole, the variation in size was much greater than normal throughout the whole section but especially in the posterior columns. Increase of Deiter's cells was not a marked feature.

"In the more intensely sclerosed portions, the tissue was filled with granular-looking material, and collections of this same material were especially noticeable around the small arteries. The *walls of the arteries* themselves in the sclerosed areas were, as a rule, *markedly hypertrophied*. The same was true of the central artery and the arteries of the nerve roots.

"Here and there in the posterior nerve roots were seen collections of corpora amylacea, or at least homogenous pale bodies of about their size."

Summary: In brief, the pathological changes seem to have been a sclerosis of the posterior columns of the cord and of the motor tracts of the lateral columns together with a destruction of nerve fibres in the posterior cornua and to a certain extent in the anterior cornua, although many of the nerve roots in the latter were comparatively healthy. This increase of connective tissue, however, was not scattered irregularly through the cord as in disseminated sclerosis, but was continuous throughout the length of the columns; nor was it by any means confined to the posterior columns as in the classic locomotor ataxia. The disease seems

rather to indicate an *incompleteness of nerve or cell development* in certain well-defined portions of the cord.

Case IV. Jessie, aged twenty-six, began to notice at the age of eight the same ataxia that she had seen in her three older sisters. She did not have the premonitory symptom of palpitation of the heart but has had marked cardiac trouble in recent years. Has had rheumatic fever twice. An examination of the heart showed signs of hypertrophy with an apex murmur transmitted to the back (mitral). There was also a venous hum in the carotids, showing a marked anæmia of the system. The ataxia in the beginning was unattended by other symptoms and gradually invaded the upper extremities, but has never been so pronounced in them as in the lower limbs. She had not and never did have "wrist drop." She could extend the arm level with the shoulder but not steadily — there was a marked muscular tremor. There was a tremor also of the head whenever she attempted to move it or perform other voluntary movements.

In the lower extremities the ataxia had progressed so far that she had been unable for years to walk without the assistance of the chairs and tables in the room and even then often falls helpless to the floor. Her gait resembled the spastic gait seen in disease of the lateral columns. She could get no aid from a cane, because she could not direct it properly. She could turn around only with the greatest difficulty and fell immediately if she closed her eyes. She complained of a feeling of cushions under the feet. In descending the stairs she always puts the right foot forward and it involuntarily jerked up and down as though it were suspended by a spiral spring. All her movements were of necessity slow and methodical.

There did not seem to be any muscular paresis, but only a lack of coördinating ability. There were no

contractures and she had never had muscular spasms. Muscular irritability was decreased to both the faradic and galvanic currents and this decrease was more pronounced on the right than on the left side, and in the lower than in the upper extremities. The tendon reflexes were absent, but plantar reflexes present. There was a right lateral deviation of the spine and a *tendency* to cyphosis. Of recent years she had complained of neuralgic pains in the lower limbs, but had only a very slight and infrequent girdle sensation. The sensibility of the skin was so decreased that, like her sister Clara, she was unable to distinguish between pinching, pricking and rubbing it, but there had never been any formication. There was no deafness, no atrophy of optic disk nor indistinctness of vision, but there was a slight nystagmus.

Under the influence of an abundant, nourishing diet and of occasional small doses of nitrate of silver, her condition in June, 1885, shows an improved tone of the system and possibly a slight amelioration of the morbid symptoms.[3]

Case V. Myra, in October, 1882, at the age of fifteen, had for more than a year been unable to walk even a short distance without unusual fatigue. She had right lateral curvature of the spine and a gait that was clearly ataxic. The tendon reflexes were normal and the only sign of impairment of the functions of the upper extremities was a slight waving in the lines of her handwriting. Reactions to electrical currents were normal. She had never complained of girdle or neuralgic pains but had felt at times a tendency to stand upon the toes instead of squarely upon the feet and always walked with irregular speed, a few hurried steps alternating with a slower movement.

She was taken from school and in June, 1885, remains in practically the same condition as when I first

[3] I showed her to the Society at the reading of my paper.

saw her, her symptoms showing no very great progression. The tendon reflex has, however, disappeared but the plantar reflex is still present. Considerable ataxia can still be detected although the gait is considerably improved.

Case VI. J. W. W., farmer, aged sixty-six, was prostrated in January, 1884, with an acute attack of rheumatism, involving principally the knees and ankles. He had been cutting ice the previous week and had thoroughly wet and chilled his legs. A severe gastritis speedily followed and lasted for about three weeks. For many years he had been subject to occasional nausea and vomiting and to habitual constipation. He had never had any colic pains nor any impairment of motion in either the upper or lower limbs, even at the time when lead was found in the drinking-water. But now he began to complain of weakness in the legs and an œdema in them at night. The heart, upon examination, was found to be dilated and irregular in its action, but free from valvular lesions. The urine per diem was about one half the usual amount and contained mucus, bacteria, and calcic oxalate crystals in great abundance. No casts. Sp. gr. 1020.

He soon began to complain of a constant prickling sensation in the feet and legs, but has never complained of fulgurating pains. As one of the *earliest* symptoms, he spoke of a girdle sensation around the body and of a feeling of heat in the same area. The gastrocnemii muscles were tense and tended to elevate the heel. It was only with the greatest difficulty that he could manage to walk, and he always felt as though he were treading on velvet. He was obliged to use two canes. The gait was purely ataxic. To turn around quickly, or to stand with the eyes closed, were acts that were equally impossible to him. Vertigo was a constant symptom but was greatly increased when

he was standing. At the base of the brain there was a "burning" sensation, as he described it, and his wife often found him in his sleep pressing the back of the neck with his hands.

The muscular weakness, but not the ataxia, quickly invaded the upper extremities and affected chiefly, if not wholly the flexor muscles. The tendon reflexes were present and electrical reactions normal or even slightly increased. Of the eyes I made no careful examination, both on account of his age and because they were seriously injured years ago by an explosion of gunpowder.

Under treatment with the nitrate of silver (gr. one half combined with extracts gentian and nux vomica, three times a day) continued for periods of three weeks and then omitted for equal lengths of time, the girdle pain together with the muscular weakness and ataxia almost wholly disappeared for the space of four months. In December, 1884 the ataxia began to return, but under treatment speedily disappeared again.

This case in its details differs somewhat from the manifestations of the disease as it has appeared in its early stages in the girls of the family, but is especially noteworthy from the fact that in the majority of the few recorded cases of this degenerative disease the initiatory symptoms have appeared prior to the age of twenty, and in none later than the age of twenty-four. (See table at end of paper.)

Differential Diagnosis: The differential diagnosis of these cases is difficult and demands the consideration of many diseases. I will briefly outline some of the symptoms in these diseases that might lead to errors of diagnosis, and that *have led to such errors in past years* in some of these very patients.

Lead Poisoning: The symptoms in their order of appearance and frequency are colic, arthralgia, paraly-

sis and encephalopathia. (Tanquerel.) Lead is *always* to be detected in the urine but the blue line on the gums is sometimes absent.[4] The paralysis is confined almost entirely to the extensor muscles; is usually in the forearm and rarely becomes general, although paralysis of the lower extremities is recognized.[5] Muscular atrophy is secondary to paralysis. Electro sensibility and contractility are *markedly reduced.* All the symptoms are *rapid in invasion and disappear readily* under proper treatment.

Cerebellar Disease: This disease is characterized by a reeling, rolling gait, *not ataxic*, but compared by Hughlings Jackson to the gait of a drunkard. Vomiting and sub-occipital pain are prominent. *Tendon reflex is not abolished.* (Sepelli.) The pupils, as a rule are contracted and do not react to light. There is *no diminution either of motion or sensation.* Paralysis is *rare* until near death; if it occurs it is due to disease in other nervous tracts and is accompanied by rigidity and local spasms.

Cerebro-Spinal Sclerosis:[6] *Disseminated Sclerosis:*[7] *Insular Sclerosis:*[8] In the *ascending* form, the first symptom is a gradual loss of power in the lower limbs which later become agitated by tremors. The gait is usually *not ataxic* but more like that of general paralysis. As the disease progresses, the upper limbs and cranial nerves become involved. The *second* stage is marked by rigidity, spasmodic contractures, and an aggravation of the tremor. Electro and reflex irritability are greatly *increased.* Epileptiform and apoplectiform attacks occur.

[4] S. G. Webber, Lead Paralysis. Reprint from Arch. of Med., vol. viii, No. 1, August, 1882.
[5] F. Minot, Bos. Med. and Surg. Journal, March 10, 1881.
[6] Charcot, Gaz. des Hôpiteaux, 1868.
[7] Bourneville et Guérard. De la Sclérose en plaques disseminees. Paris, 1869.
[8] Moxon, Guy's Hosp. Reports, vol. xx, 1875.

In the *descending* form, on the contrary, the tremor is the primary symptom and is first noticed in the muscles controlled by the cranial nerves. In the *second* stage there is paresis of the upper and later of the lower limbs with permanent contractures.

In the *third* stage of both forms there are *incontinence of urine and fæces, bed sores*, facial paralysis and dementia. The microscope shows a degeneration *irregularly* scattered through the motor tracts of the brain and antero-lateral columns of the cord.

Antero-Spinal Paralysis: (Anterior Poliomyelitis, Erb.) The invasion of paralysis is usually *sudden* during an acute attack of fever although it may be without fever. The paralysis attacks the lower extremities and extends upwards involving the muscles of respiration and deglutition.[9] It is complete but *soon partially disappears*. There is *rapid muscular atrophy* differing from progressive muscular atrophy in being *secondary* and in involving *whole groups* of muscles. Electro irritability is early lost. There is *no anæsthesia*, incontinence or paralysis of sphincter ani, differing thus from general myelitis.

Diseases of the Lateral Columns: The positive symptoms are paresis with rigidity and contractures (often talipes equinus) and an *increase of all forms of reflex excitability*, especially in the tendons. Among the negative symptoms is the absence of muscular atrophy, of *ataxia*, and of cerebral, rectal and vesical complications. In the more common variety, Tabes Dorsalis Spasmodique, of Charcot,[10] Spasmodic Spinal Paralysis, of Erb,[11] Tetanoid Paraplegia, of Seguin, initial sensory symptoms have been reported. Then come the paresis, motor irritation, the *spastic gait* and

[9] Duchenne, De l'electrisation localisée. Paris, 1872.
[10] Leçons sur les Malad. du Syst. Nerv. 4me fasci.
[11] Virch. Archiv., Bd. lxx, Heft 2.

contractures. No autopsies have been reported, however, which reveal uncomplicated lateral degeneration.

Antero Lateral Spinal Sclerosis: This begins without fever and is characterized by *loss of power in the upper extremites* followed by a *general atrophy of the muscles* of the paralyzed limbs, "*atrophie en masse*," of Charcot. *Later*, the lower limbs are similarly invaded and in a greater degree. The cranial nerves are speedily involved so as to simulate bulbar paralysis. *Muscular coördination is intact.* There are *no neuralgic pains.*

Chronic Myelitis: There is a tingling spinal pain and girdle sensation but *no neuralgic pains* in the extremities. Electro contractility and reflex excitability are markedly *increased.* Paralysis of motion and violent muscular spasms in lower extremities. The functions of bladder and rectum are *disordered.*

Pseudo Hypertrophic Muscular Paralysis: Is an hereditary *disease of infancy*, expressed by *increase of volume* and hardness of certain muscles, especially in the lower extremities; by *secondary atrophy and paresis* and by conservation of cutaneous sensibility and the functions of the bowel and bladder.[12]

Progressive Muscular Atrophy: Atrophy of muscles in hand and fore arm, "main en griffe" is the first marked symptom, although a slight loss of power in the upper extremity may be early noticed.[13] The atrophy is rarely symmetrical and may invade muscles in all parts of the body.[14] Paralysis is always *secondary* to atrophy and finally invades the muscles of respiration. Electro contractility is decreased but not abolished.

Locomotor Ataxia: The introductory stage which

[12] Nervous Diseases. A. McL. Hamilton. page 311.
[13] Roberts. Essay on Wasting Palsy, London, 1858.
[14] Cruvelhier. Arch. Gén. de Méd, May, 1853.

often lasts for years is characterized by *lancinating neuralgic pains* in the lower extremities, in the trunk (generally) and in the upper extremities (more rarely); by *paræthesia* and often *anæsthesia of the lower extremities*, by *girdle pains*, motor disturbances, gastralgia and *irritability of bladder* and sexual organs. There is often amblyopia, diplopia, or amaurosis with marked head symptoms. The tendon reflexes begin to disappear.

In the fully developed disease, which may last from five to twenty years, there is an increase of all these symptoms with ataxia of the lower extremities. Later this ataxia may in some cases invade the upper extremities. The gross strength of the legs is unreduced. The tendon reflexes are lost but *electro irritability is preserved* and often greatly *increased*. There is *atrophy of the optic disk*. The final stage is short and is characterized by paresis and contractures, by muscular waste, by *bed sores* and *paralysis of sphincters of bowel and bladder*. Death is either by exhaustion or some intercurrent disease.

Degenerative Ataxia: The introductory symptoms of this complex disease which we have been considering are slight, and consist for the most part of dyspnœa and an irritable heart and stomach. Occurring in girls and before or at the age of puberty, they might easily be confounded with the ordinary symptoms of anæmia and escape particular notice. But the patient is conscious of a certain *weakness in the lower limbs* which renders the movements of the feet hesitating and uncertain. Sooner or later this irregularity of motion becomes apparent to others. The tendon reflexes have not yet been affected. There are *no lancinating or girdle pains*, and *no disorders of sensation*. Such symptoms may last with little change for months or even years.

The first stage of the disease is characterized by a gait that is clearly *ataxic*. Not only has standing become a difficult act but turning around is still more difficult. The motor incoördination which at first affected only the lower limbs has extended gradually *to the upper extremities*. There are irregular *oscillations of the head* that are aggravated in their severity by attempts at voluntary movement in any part of the body. Whether the wrist drop that was observed in two of these cases is a symptom of the spinal disease may well be called in question, since we have evidence of lead poisoning in the family some years ago.

In the father, the girdle pain was one of the earliest symptoms, but in all the other cases it has occurred *very late* in the disease. Nor is this the only symptom that distinguishes this form of ataxia from the classic locomotor ataxia. There are *few, if any disorders of sensation*, such as wandering pains or anæsthesia. There may, however, on the contrary, be hyperæsthesia. The *tendon reflexes disappear* in time, as do also the electro reactions of sensation and muscular irritability. Strange to say, the *plantar reflexes may be retained*. This stage will last for years with little change, temporary improvements alternating with speedy relapses.

The second stage marks the fully developed disease. The incoördination has progressed so far that both *walking and standing have become impossible*. Nor is it any longer possible to execute free movements with the hands or arms, to work or feed one's self. The unfortunate sufferer must sit or half recline, a helpless burden in a chair. Yet there has *not been a true or complete paralysis*. *Muscular atrophy and contractures* begin to be well marked and produce a great distortion of the limbs. The *skin is anæsthetic* but is of fair vitality, and *pressure sores do not occur*. The *speech*

has a peculiar drawl and finally becomes unintelligible. The signs of bulbar paralysis appear. *Neuralgic and fulgurating* pains begin to be distressing, and the attacks of dyspnœa and collapse are frequent. There is *no paralysis of the sphincters* and little if any irritability of the bladder.

The final stage is brief. The patient is confined to the bed a few weeks only and in the two girls of this family that have died, the symptoms were those of meningitis and an acute myelitis affecting the lateral columns. The probability nevertheless exists that some intercurrent disease rather than the spinal degeneration would prove in many cases the actual cause of death.

Causation. The causation is obscure. No differentiation of the disease from complex cases of the ordinary locomotor or progressive ataxia of Duchenne was made until 1861, when Professor Friedreich of Heidelberg presented six cases which seemed to require a new and separate classification. It was not, however, until 1863 that these observations were published[15] and I can find by the most careful study only forty-three cases upon record that unquestionably agree with Freidreich's in clinical and pathological history.[16]

The disease has been called hereditary but the cases of *direct* transmission are very few. It is certainly, however, *a family disease*, and in the majority of the recorded cases there has been found in the parents not an ataxia, perhaps, but certain mental and nervous peculiarities. Above all causes Brousse[17] mentions alcoholism and consanguineous marriages, and in my

[15] Ueber degenerative Atrophie der spinalen Hinterstränge. Virch. Archiv., Bd. 26, Bd. 27.

[16] Since the writing of this paper Dr. J. J. Putnam has showed me notes of two cases that he has seen and Dr. E. C. Seguin has reported six cases in the New York Medical Record, June 13, 1885. See Table of Cases.

[17] De l'Ataxie Héréditaire.

cases the history of alcoholism in previous generations is well established. Seeligmüller [18] noticed in his cases habits of onanism. I made careful investigations to detect this habit in my patients, and believe I am justified in saying it did not exist. Even if it did, it may not bear a causative relation to the disease.

According to Friedreich the disease is one of puberty. The age at which the initiatory symptoms occur varies, however, from four to twenty-four years, while in one of my cases it was undoubtedly sixty-six. The sexes seem to be about equally affected, although the majority of my cases were females.

Treatment. The treatment is rather unsatisfactory. Little or no hope can be entertained of permanent recovery, and the most that can be done is to render the condition of the patient comfortable. Cod liver oil, if the stomach will bear it, and concentrated animal foods are absolutely essential to maintain the physical strength. Iron I found to be ineligible, nor did I succeed any better with the vegetable tonics. Phosphorus for a time worked well, but its effects were transient at the best. In the nitrate of silver well pushed and the application of electricity, I consider we have the two best means of giving relief that are really practicable and available. Persistent cauterization over the spinal column has been reported to be attended with good results, but private patients are few who would submit to the procedure.

[18] Hereditäre Ataxie mit Nystagmus. Arch. f. Psych. und Nervenk, Bd. x., Heft. i.

Table of Cases of Hereditary Ataxia.

No.	Observer.	No. in same Family.	Sex.	Date of first symptoms.	Family History.
1	Friedreich	2	M	18	Heredity; mother hemiplegic; father a drunkard.
2	. . . .		F	18	
3	. . . .	4	F	16	Heredity; mother of limited intelligence; father a drunkard, and died of phthisis.
4	. . . .		F	16	
5	. . . .		F	15	
6	. . . .		M	15	
7	Eulenberg	3	F	13	No special heredity; five brothers and sisters died young.
8	. . . .		F	13	
9	. . . .		F	13	
10	Carre	7	M	—	Direct heredity; mother, grandmother and an uncle ataxic.
11	. . . .		M	—	
12	. . . .		F	—	
13	. . . .		F	—	
14	. . . .		M	—	
15	. . . .		M	—	
16	. . . .		F	22	
17	Quincke	2	M	6	No heredity; father a drunkard, other family history good.
18	. . . .		F	8	
19	A. Carpenter	2	F	—	Family history good.
20	. . . .		F	—	
21	J. H. Kellogg	2	M	6	Heredity; an ataxic brother died at 20, and several cousins had similar disease.
22	. . . .		M	6	
23	Gowers	5	M	19	Heredity; mother had chorea; one brother and two half cousins insane.
24	. . . .		F	18	
25	. . . .		M	19	
26	. . . .		M	—	
27	. . . .		M	—	
28	Seeligmüller	2	M	12	Consanguinity and some nervous peculiarity in family, but no ataxia.
29	. . . .		M	12	
30	Schmid	2	M	12	Father a drunkard; other family history good.
31	. . . .		M	11	
32	Brousse	1	F	24	Direct heredity; grandmother died of phthisis; mother, of ataxia; father, of cerebral softening.
33	Rütimeyer	8	M	14	History in family of various nervous affections, chorea and poliomyelitis.
34	. . . .		M	7	
35	. . . .		F	6	
36	. . . .		M	7	
37	. . . .		M	7	
38	. . . .		F	5	
39	. . . .		M	4	
40	. . . .		M	4	

TABLE OF CASES OF HEREDITARY ATAXIS,—*continued*.

No.	Observer.	No. in same Family.	Sex.	Date of first symptoms.	Family History.
41	. . . .	3	M	7	Father and mother were drunkards.
42	. . . .		M	7	
43	. . . .		F	7	
44	W. E. Smith	6	F	6	Some hereditary influence; grandfather died with ataxic symptoms; history of alcoholism.
45	. . . .		F	5	
46	. . . .		F	9	
47	. . . .		F	8	
48	. . . .		F	13	
49	. . . .		M	66	
50	J. J. Putnam[19]	2	M	7	No history of heredity; history of neglect and malnutrition; followed scarlet fever in the boy.
51	. . . .		F	6	
52	E. C. Seguin	3	F	4	No heredity; family history remarkably good.
53	. . . .		M	10	
54	. . . .		F	7	
55	. . . .	3	F	15	Mother died of consumption; other family history good.
56	. . . .		M	7	
57	. . . .		M	15	

[19] Since the writing of this paper, Dr. J. J. Putnam has showed me notes of two cases that he has seen, and Dr. E. C. Seguin has reported six cases in *New York Medical Record*, June 13, 1885.

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